REMARKS

Reconsideration of claims 29, 35, 36 and 40-44 is respectfully requested. Claim 37 is canceled. Claims 1, 6-8, 13 and 25-27 are withdrawn.

The rejection of claims 29, 35, 36 and 40-44 under 35 U.S.C. 112, first paragraph is respectfully traversed. The examiner's reliance on *University of Rochester v. G.D. Searle* and *University of California vs. Eli Lilly and Co.* to support the rejection is misplaced and improper given the written description of the term "organic, nitrogen-containing preservative agent" in the application on page 9, paragraph [0038]. The issue of whether a patent specification adequately describes the subject matter claimed is decided on a case-by-case basis, and accordingly, is a question of fact. *Vas-Cath, Inc. v. Maharkar*, 19 USPQ2d 111 (Fed. Cir. 1991). One begins a §112, first paragraph analysis by reading the relevant disclosure in light of the knowledge possessed by those skilled in the art. That knowledge can be established by reference to the patent literature that was published prior to the filing date of the application.

In this case, the person of ordinary skill is likely one with five or more years of experience in developing topical pharmaceutical formulations that require a preservative agent, and particularly a person developing preserved ophthalmic formulations. This person, having read the application in its entirety, and in particular, paragraph [0038] in the context of the application and the art of ophthalmic formulations would have absolutely no difficulty in understanding what is meant by the term "organic nitrogen-containing preservative agent". This is particularly true given the list of specific species cited in paragraph [0038]. In fact, based on the cases and specific portions thereof cited in support of the rejection, one must come to a different factual conclusion than that presented by the rejection. As stated, a "description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus." Office Action page 3. In this case, the recited structural feature of the recited preservative agents" are "organic, nitrogen-containing" agents.

Nitrogen-containing preservative agents are well recognized in the art of topical formulations, going back thirty years to the development of poly(hexamethylane biguanide) and polyquaternium-1 in the early 1980's, and benzylalkomium chloride before that. Again, this term must be viewed by one of ordinary skill in the art, and in the context of the application as a

whole, not in a vacuum. Applicants invite the examiner to search the term "preservative agent" as related to ophthalmic compositions, or simply, review the secondary reference cited in the Official Action, U.S. Pat. No. 5,872,086, column 5, lines 6-26.

For the reasons stated, Applicant respectfully requests that the rejection under §112 be withdrawn.

The rejection of claims 29 and 40-44 under 35 U.S.C. 102(b) as anticipated by Cini et al (U.S. 5,130,298) is respectfully traversed. The rejection characterizes Cini as describing a composition comprising zinc-EGF at 5mM to 20mM and cites to column 4, lines 35-51. Given this characterization, the rejection under §102 is improper and Applicants respectfully request that the rejection be withdrawn.

Let's assume one prepared a zinc-EGF solution containing 250 micrograms/mL, and stabilizes such a solution with 10 to 20 mM zinc. The 10 mM of zinc corresponds to 654 mg of zinc in a one liter solution, which corresponds to 0.065 wt% zinc. The claimed compositions require slightly less amounts of zinc, that is, from 0.001 wt% to 0.05 wt.%. The claimed compositions also require an organic, nitrogen-containing preservative agent, which is not described in Cini. Cini merely describes the use of preservatives, column 5, line 55, and then goes on to recite a few, column 5, lines 59-60. In fact, none of those preservatives are organic nitrogen-containing preservative agents.

For a reference to anticipate a claim, the reference must disclose all of the claimed elements. Also, the reference must "sufficiently describe the claimed invention to have placed the public in possession of it." *Minnesota Mining of Mfg. v. Johnson & Johnson Orthopedics, Inc.*, 24 USPQ2d 1321, 1332 (Fed. Cir. 1992). Moreover, the reference must "clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound [composition or formulation] without any need for picking, choosing and combining various disclosures. In re Arkley, 172 USPQ 524, 526 (CCPA 1972).

If one applies the law of anticipation summarized above to the generalized disclosure cited in Cini, one can only conclude as a matter of law that claims are not anticipated. Each and every claim limitation, for the reasons stated above, are not described in Cini with sufficient specificity. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The rejection of claims 35-37 under 35 U.S.C. 103(a) as obvious over Cini in view of Ellis et al. (U.S. 5,872,086) is respectively traversed.

As stated, Cini teaches a composition containing zinc-EGF, and such compositions can be used as an ophthalmic composition, e.g., eye drop or eye gel. The focus in Cini, however, is on the preparation of stable EGF formulations. At the time Cini was filed it was said EGF polypeptide would lose biological activity over time as the EGF degraded to multiple species. Accordingly, EGF formulations lacked long term stability making such formulations impractical. See, Cini, col. 1, lines 26-51. Cini is said to have solved the stability problem associated with EGF-formulations by stabilizing the EGF polypeptide with zinc cation. "It has been determined that maximum stability of EGF is obtained when about 10-20 mM of zinc cation is added to an aqueous solution of EGF." Cini, col. 4, lines 35-37.

The rejection asserts that "[i]t would have been obvious to one of ordinary skill in the art when making the composition of Cini et al., to adjust the viscosity using a polymer [described in Ellis] that has been used with similar components in ophthalmic compositions. Applicants respectfully disagree for the following reasons.

Again, the focus in Cini is on zinc-stabilized EGF formulations, yet the examiner points to a single statement regarding the use of "polymers for adjusting viscosity" of such formulations to support the rejection. There are virtually hundreds of different polymers that can be used to increase the viscosity of ophthalmic compositions. Applicants ask what is so special about cationic cellulosic polymers, and why would one of ordinary skill choose the polymers of Ellis over any other? Is there some teaching or suggestion in either reference that cationic cellulosic polymers provide additional benefit to polypeptide compositions over other polymers? Is there any teaching in either reference that cationic cellulosic polymers should be used if zinc is present in the ophthalmic composition? The answer to both questions is no; there is no such teaching.

Even following *KSR International* rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. See, *In re Kahn*, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006); MPEP 2142, 2143. Applicants submit that there exists no rational underpinning to support the mere combining of Cini with Ellis. As stated by the Court in *KSR*, "a patent composed of several elements in not proved obvious merely by demonstrating

that each of its elements was, independently, known in the prior art." In other words, why would one of ordinary skill wishing to adjust the viscosity of Cini's zinc-EGF formulations choose a cationic cellulosic polymer over a non-ionic cellulose or anionic cellulose or any of the many non-cellulosic biopolymers? The only direction provided to the examiner in the selection of a cationic cellulosic polymer over all the other viscosity inducing polymers is the application at issue, and we know any rejection based on such an analysis is improper and must be withdrawn.

The *KSR* Court also suggests that one way to show obviousness is to note that at the time of the application "a known problem [existed] for which there was an obvious solution encompassed by the patent's claims." In this case, the problem sought to be solved by Applicants was to enhance the preservative efficacy of ophthalmic compositions that contained an organic nitrogen-containing preservative agent. Applicants submit that neither reference mentions this problem, nor more importantly, Applicants question whether such a problem was even recognized in the art of developing preserved ophthalmic compositions.

Applicants inventive compositions solve this problem by adding small amounts of zinc (0.001 wt% to 0.05 wt%) and a cationic cellulosic polymer to the composition. Compare the Preservative Efficacy (PE) Results of Example 6 to Example 8 and Example 7 to Examples 9 and 10.

In view of the foregoing arguments and amendments, Applicant believes that the application is in condition for allowance. An early and favorable action on the merits is solicited.

Respectfully submitted,

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